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(54) Title: PREPARATION

(57) Abstract

The invention relates to the use of monophasic zinc hydroxycarbonate as antimicrobial agent in personal care products, particularly in such products which also contain a surfactant such as a soap or a synthetic detergent. The invention also relates to a process for making the zinc hydroxycarbonate, whereby a solution of a soluble zinc salt and a solution of alkalimetal carbonate are fed simultaneously into a precipitation vessel to form a precipitate of monophasic zinc hydroxycarbonate.

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PREPARATION

INTRODUCTION

This invention relates to preparation of zinc hydroxycarbonate and antimicrobial compositions containing that compound.

This invention particularly relates to:

a) preparation of monophasic zinc hydroxycarbonate suitable for use in personal care products such as toilet soaps and cosmetics like skin, scalp and/or hair products and dental products such as toothpastes, toothpowders, dental creams and

b) personal care compositions such as toothpastes, toothpowders, toilet soaps, skin creams, skin powders, deodorants, antiperspirants and hair care products comprising zinc hydroxycarbonate as an antimicrobial agent.

BACKGROUND

Zinc hydroxycarbonate occurs in nature in the mineral hydrozincite. Generally sulphide ore bodies are overlain by deposits of smithsonite, calamine and hydrozincite. Franklinite, willemite and zincite occur in white crystalline lime stone in some places. Calcite, dolomite and sometimes quartz occurs as materials associated with zinc blend or sulphide. The monophasic zinc hydroxycarbonate prepared by the process of present invention has a structure similar to that of hydrozincite without any other impurity phases as may be present in the mineral.

Basic zinc carbonate may be represented by

$Zn_4(CO_3).(OH)_6$. or $Zn_5(CO_3)_2.(OH)_6$

and sometimes it is accompanied with ZnO.

The monophasic zinc hydroxycarbonate of the present invention has the following formula

$$Zn_5(CO_3)_2.(OH)_6.x\ H_2O \quad (x = 0\text{-}4)$$

It is known that divalent zinc ions can provide antimicrobial activity. If they are made available freely in soaps or cosmetic or dental formulations, they would contribute to the health care features of these products. But the zinc ions tend to affect colour, perfume, flavour, and/or taste of the cosmetic products, dental products or soaps, and they may reduce the shelf life of such products. Due to the structure of the hydrozincite (in which zinc is present in the form of stable covalent complexes), free divalent zinc ions are not made available in the product. Thereby the shelf life of the health care products is improved. Zinc hydroxycarbonate is also an antimicrobial compound, and it is surprisingly found that when a personal care product containing it comes into contact with the skin or with the saliva in the mouth, or the microflora of the skin, scalp or hair, the zinc hydroxycarbonate in the presence of a surfactant such as soap and/or synthetic detergent shows a synergistic enhancement of the antimicrobial effect. Further its substantivity keeps it on the body to readily deliver free divalent zinc ions to act as antimicrobial agent at the site as and when desired. It is hypothesised here that the zinc hydroxycarbonate, not being soluble in water, is substantive to the skin, mucous membranes, hair, mould and microbial cell walls particularly wherever there is any acid site, and upon neutralising the acid site delivers divalent zinc ions which act on microbes which generate acids such as butyric and lactic acids. The surfactant, e.g. soap and/or synthetic detergents place the zinc hydroxycarbonate onto the desired spot. Thus, it is thought that the combination

not only gives synergistic effect in antimicrobial activity in use but also gives triggered release effect during the intervening period inbetween successive application of the products containing it. Thus, zinc hydroxycarbonate acts as an agent to generate active antibacterial/antimicrobial species - divalent zinc ions - by its synergistic combination with surfactants such as soaps/synthetic detergents.

PRIOR ART

There are processes known for the preparation of basic zinc carbonate. Preparation of monophasic zinc hydroxycarbonate suitable for use in personal products has not been described. Use of mineral hydrozincite in dental preparations has been reported, but synergistic antimicrobial compositions containing zinc hydroxycarbonates have not been reported in the literature. In a Russian process degradation of zinc ammonium carbonate complexes with hot moist air in the presence of lignin sulphonate gives zinc hydroxycarbonate. [Krechmer G.A.; SU 664923 (30 May 1979)].

In another Russian process, basic zinc carbonate is prepared by an electro-chemical process from an electrolyte containing sodium nitrate and sodium bicarbonate. [Oratovskii V.I.; SU 447366 (22 August 1975)].

In another process, zinc hydroxide (a waste product from the production of $Na_2S_2O_4$ was used as raw material for the production of basic zinc carbonate ($ZnCO_3.3Zn(OH)_2$) by carbonation. [Telepneva A.E. and Artemova V.A., Tr. Ural. Nauch.-Issled. Khim. Inst. 1973, 24, 26-8].

Further prior art references are:

a. Inst. Francais Du Petrole; EP 0155868 (20 February 1985)

This reference describes a process for the preparation of catalysts for synthesis of methanol from carbon oxides wherein a mixture of hydroxycarbonates of copper/zinc/aluminium/rare earth metal and/or zirconium is prepared by a co-precipitation technique. In this process soluble salts are dissolved together and reacted with ammonium, sodium, potassium carbonates, and/or hydroxides n the pH range 6.3-7.3.

b. Fuji Chem. Ind. Co.; JP 5025052 (2 February 1993)

This reference describes the preparation of an antimicrobial drug comprising supplying continuously aluminium, an aqueous solution of antimicrobial metal salts (including copper, zinc, magnesium, nickel and cobalt), sodium carbonate solution and sodium hydroxide solution into a reaction tank at room temperature keeping the pH of the reaction solution at 7 to 11 by adjusting the NaOH addition, filtering the reacted suspension, rinsing with water and drying. The molar ratio of aluminium and copper ion salt is 1:1 to 4:1.

c. Vian A. et al., An Quim. Ser. A., 1984, 80(3) Suppl. 2, 724-31 (Spanish) [CA: 103: 89773v]

According to this reference, in connection with recovery of zinc from ion-exchange wash liquors, used in the leaching of pyrite cinders, NaOH, $Ca(OH)_2$, and $A(OH)$-Na_2CO_3 mixture, (where A = Na, K, NH_4) were used to precipitate zinc from zinc chloride solution. While NaOH produced a precipitate consisting of [ZnO and $Zn_5(OH)_8.Cl_2.H_2O$], $A(OH)$ and Na_2CO_3 mixtures gave a precipitate consisting mainly of [ZnO and

$Zn_5(CO_3)_2(OH)_6$] with various proportions.

In French patent 2493704, the use of natural carbonates forming an isomorphic series with the calcite, more resistant to acids than Iceland Spar (this includes natural hydrozincite) has been reported for treatment or prevention of the troubles from demineralisation of hard tissues such as teeth.

DEFINITION OF THE INVENTION

Accordingly, the present invention relates to

a) a process for the preparation of monophasic zinc hydroxycarbonate suitable for use in personal care products and

b) antimicrobial personal care products such as toothpastes, toothpowders, soaps, skin cream, skin powders, deodorants, antiperspirants and hair care products comprising zinc hydroxycarbonate, and a surfactant such as soap or a synthetic detergent.

The process of the present invention for the preparation of zinc hydroxycarbonate, (suitable for use as antimicrobial agent in personal care compositions such as soaps, cosmetic - skin and hair- and dental formulations) comprises

(i) dissolving a soluble zinc salt in water and heating it, to keep the solution warm before use,

(ii) dissolving an alkali metal carbonate, such as sodium potassium or ammonium carbonate, in water,

(iii) taking water in a precipitation vessel and maintaining it at 35-95 °C,

(iv) pumping warm solutions of (i) and (ii) into the precipitation vessel simultaneously, and maintaining the temperature at 50-98 °C with continuous stirring and warming if necessary,

(v) filtering off the precipitate and washing it with water until it is free from anions, and

(vi) drying the washed material.

The soluble zinc salt may be chloride, sulphate or nitrate. The pH of the reaction is between 8-10; preferably about 9.

The preferred temperature of the precipitation reaction is 50-98 °C; more preferred is 80-90 °C.

The product of the reaction is air dried at temperature upto 150 °C. Vacuum drying may be used.

The precipitated basic zinc carbonate obtained by the process of the invention was identified by XRD, IR, SEM Morphology and its Zn content was found to be between 54.75 to 59.55 %. The chemical formula was found to be

$$Zn_5(OH)_6(CO_3)_2.X.H_2O$$

X varies between 0 and 4 depending on the drying temperature and duration of drying.

The antimicrobial personal care compositions of the invention comprise from 0.1 % to 20 % by weight of monophasic zinc hydroxycarbonate in combination with the usual ingredients of personal care compositions comprising a soap or detergent, with or without other antimicrobial agents.

DETAILS OF THE INVENTION

If the sodium carbonate solution is taken in the precipitation vessel initially, and zinc salt solution is thereafter pumped into it or vice versa, the material obtained is not suitable for cosmetic use. It is more gritty than required. On the other hand when sodium carbonate solution and the zinc salt solution are simultaneously pumped in the precipitation vessel, the physical properties of the material obtained are very close to the requirement of the formulations.

When the zinc hydroxycarbonate is prepared as above by precipitation at different temperatures viz., 50, 70 and 85 °C it has been found that all these products exhibit a hydrozincite structure. However, when it is precipitated at room temperature, the product is not monophasic.

Synergistic action of zinc hydroxycarbonate with soaps containing TCC (trichlorocarbanilide) is another facet of this invention.

Synergistic action of zinc hydroxycarbonate with toothpastes containing soaps and/or detergents such as sodium ricinoleate, sodium lauryl sulphate, is yet another facet of this invention. Zinc hydroxycarbonate shows synergistic antimicrobial activity in toothpastes with any abrasive agents such as chalk, silica, dicalciumphosphate dihydrate (DCPD), alumina trihydrate.

The zinc hydroxycarbonate neutralises organic acids such as lactic acid as and when they are generated in the mouth, and the release of zinc ions is triggered off as a result of this neutralisation of zinc with e.g. lactic acid acting on oral microflora. This process is likely to help to reduce plaque pH and buffer the plaque. This is another facet of the invention.

Synergistic action of zinc hydroxycarbonate with detergent and/or antidandruff actives like zinc pyrithione in shampoos/hair dressings is yet another aspect of this invention.

Synergistic action of zinc hydroxycarbonate in skin cream and talcum powder is yet another example of this invention. It has the added advantage of reducing body malodour caused by some of the fatty acids, hydroxy acids and their breakdown products, present in body malodour.

The neutralisation of organic acids such as butyric acid generated on skin which is responsible for malodour by the zinc hydroxycarbonate release zinc ions acting on the skin microflora. It also acts as a buffer to control the pH in the area of its action on skin. The synergistic compositions such as deodorants, antiperspirants are based on this principle and it is another facet of the invention.

EXAMPLES

The invention will now be illustrated by way of Examples. The Examples are for illustration only and they do not in any way restrict the scope of the invention.

Example 1: Preparation of monophasic zinc hydroxycarbonate

Materials used in this Example were of technical grade.

1. Zinc sulphate heptahydrate (300 g) was dissolved in water (1000 ml). Sodium carbonate (150 g) was dissolved in water (1000 ml).

2. In the precipitation vessel (5000 ml) 200 ml water was taken and maintained at 85 °C.

3. Warm solutions of zinc sulphate and sodium carbonate

were pumped into the precipitation vessel simultaneously maintaining the precipitation temperature at 85 °C, with continuous stirring.

4. When all the solutions were added and the precipitation completed, the precipitate was filtered through a Buchner funnel, and washed with hot (60 °C) water (2000 ml).

5. The product was dried in an air oven at 110 °C for six hours. Yield: 125 g (100 %).

Analysis of the product:

Zn content:
55 % by wt. (EDTA Titration using Eriochrome Black T)

Surface Area:
80 m^2/g (BET method)

X-Ray (powder) diffraction pattern:
it indicated a highly crystalline nature of the product and it was isostructural with the mineral hydrozincite.

FT-IR Spectra:
it indicated a basic carbonate group. [- absorption doublets at 1507 and 1385 cm^{-1}. This was confirmed by adsorption maxima at 1046 (bridging type OH: bending mode); at 835 (out-of-plane CO_3 deformation); at 708 (in-plane CO_3 deformation) and at 470 cm^{-1} (ZnO symmetric stretching)].

Example 2: Evaluation of soaps containing zinc hydroxycarbonate

Soaps containing monophasic zinc hydroxycarbonate (ZHC) with and without trichlorocarbanilide (TCC) were evaluated for their antibacterial activity by the Bureau of Indian

Standards' Test method given in IS 11479 - 1985.

Results are given in Table 1.

Table 1

Composition	Substantivity
1. Soap base*	No
2. Soap base + 0.1 % TCC	No
3. Soap base + 0.5 % ZHC	No
4. Soap base + 0.1 % TCC + 0.5 % ZHC	Yes

* Soap base used in these compositions had 55 % TFM (12.5 % CNO); 24 % Structurant(talc); 1.5 % Tetrasodium pyrophosphate, 0.5 % sodium carbonate.

These results clearly showed that very small amounts of TCC when mixed with small amounts of ZHC synergistically reduced the microbial activity and improved substantivity much more than either of them individually with soap base.

Example 3: Evaluation of toothpastes containing zinc hydroxycarbonates

The antimicrobial activity of the toothpaste was assessed by [the in-vitro method described below] estimating total viable count by spread plate technique as described in Medical Microbiology by R. Cruickshank, 11th Edn., 1965, pp 886-889.

The results of the assay are given in Table 2.

Table 2 Antimicrobial activity of toothpastes containing zinc hydroxycarbonate

Composition	% Inhibition
1. Toothpaste base*: (0.1 % on the broth)	23.6
2. Toothpaste base + 2 % ZHC: (0.1 % - 20 ppm ZHC - on the broth)	86.2
3. 20 ppm ZHC (as slurry) on the broth	41.3

* Composition of the toothpaste base is same as that given in Example 4A without any addition of ZHC.

The results clearly indicated that the Composition 2 had a synergistic inhibitory activity.

In-vitro method:
Appropriate dilutions of toothpaste are incubated with a *Streptococcus* spp. culture isolated from the oral microflora. An aliquot of this is taken and placed on an Agar plate for growth at room temperature overnight. The following day colony forming units (CFU) are counted. The activity is expressed as % inhibition. This is calculated based on the growth of bacteria (no of CFUs) without any treatment, which is taken as 100 % growth or 0 % inhibition.

Example 4: Toothpaste compositions according to the invention

The following toothpaste compositions were formulated as described below:

Composition	4A(%)	4B(%)
Precipitated calcium carbonate (Chalk)	40.0	----
Abrasive silica	----	10.0
Thickening silica	1.5	8.3
Sorbitol (70 %)	27.0	45.0
Sodium carboxymethylcellulose (SCMC)	0.7	0.9
Sodium saccharin	0.2	0.2
Titanium dioxide	---	1.0
Sodium lauryl sulphate	2.5	2.5
Sodium dodecylbenzenesulphonate (40 %)	1.0	0.5
Monosodium phosphate	0.4	---
Zinc hdyroxycarbonate	2.0	2.0
Flavour	q.s.	q.s.
Demineralised water to	100	100

Method of preparation

Sorbitol (70 %) and water were taken into a vacuum mixer fitted with a low speed scraper unit and a high speed homogeniser. Minor soluble compounds such as saccharin, monosodium phosphate etc. were added to obtain clear solution. The mixture was heated to 50 °C and mixture of SCMC and abrasive chalk/silica was added. The mixture was homogenised and thickening silica was subsequently added. When the mixture was of consistent quality, detergents consisting of sodium lauryl sulphate and dodecyl benzene sulphonate predissolved in water were added. The batch was cooled to 40 °C. Zinc hydroxycarbonate was then added and mixing was continued. Flavour was added last to complete the batch.

Example 5: Neutralisation of zinc hydroxycarbonate with n-butyric acid

Various quantities of n-butyric acid (0.5 % solution) were added to zinc hydroxycarbonate (5g in 30 ml slurry) and the

filtrate was analysed for soluble Zn++ ions and its pH was recorded.

Results are given in table 3.

Table 3

Mole ratio of butyric acid: ZHC	Soluble Zn++ ions in the filtrate (% zinc on ZHC weight)	pH of the filtrate
0	Nil	6.6
4	42.58	6.0
6	61.92	5.9
10	81.02	5.8
12	100.0	5.5

This Example supported our hypothesis of triggered release action of ZHC and buffering of the pH of the solution.

Claims

1. An antimicrobial personal care product comprising a surfactant and an antimicrobial agent, characterised in that the antimicrobial agent is or comprises monophasic zinc hydroxycarbonate.

2. A product according to claim 1, characterised in that the monophasic zinc hydroxycarbonate is present in an amount of 0.1 - 20 % by weight of the product.

3. A product according to claim 1 or 2, characterised in that the surfactant is a soap or a synthetic detergent.

4. A product according to claims 1-3, characterised in that the personal care product is a toilet soap.

5. A product according to claims 1-3, characterised in that the personal care product is a toothpaste.

6. A process for the preparation of monophasic zinc hydroxycarbonate, suitable for use in the products according to claims 1-5, said process comprising the steps of
   (i) dissolving a soluble zinc salt in water and heating he resulting solution,
   (ii) dissolving an alkalimetal carbonate in water,
   (iii) placing water in a precipitation vessel and maintaining the water at a temperature of between 35-95 °C,
   (iv) placing the solutions i) and ii) simultaneously into the precipitation vessel with warm water according to iii), and maintaining the temperature at 50-98 °C with continuous stirring,
   (v) filtering-off the precipitate formed during

step iv) and washing the filtrate with water until it is free from anions, and

(vi) drying the washed material.

7. Use of monophasic zinc hydroxycarbonate as antimicrobial agent in personal care product.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K7/16 A61K7/48 A61K33/30 C01G9/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K C01G

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	FR,A,2 493 704 (LE MOUEL) 14 May 1982 cited in the application see the whole document -----	1-7

☐ Further documents are listed in the continuation of box C.

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Date of the actual completion of the international search	Date of mailing of the international search report
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Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax (+ 31-70) 340-3016	Fischer, J.P.

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INTERNATIONAL SEARCH REPORT

.nformation on patent family members

Int: onal Application No
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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
FR-A-2493704	14-05-82	FR-A- 2494585	28-05-82

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